September 4, 2002

Edward W. Kordoski, MBA, Ph.D.
Executive Director
Synthetic Organic Chemical Manufacturers Association
Dibasic Esters Group
1850 M. Street, NW
Suite 700
Washington, DC 20036

Dear Dr. Kordoski:

The Office of Pollution and Toxics is transmitting EPA's comments on the robust summaries and test plan for Dibasic Esters, posted on the ChemRTK HPV Challenge Program Web site on January 30, 2002. I commend The Synthetic Organic Chemical Manufacturers Association's Dibasic Esters Group for its commitment to the HPV Challenge Program.

EPA reviews test plans and robust summaries to determine whether the reported data and test plans will provide the data necessary to adequately characterize each SIDS endpoint. On its Challenge Web site, EPA has provided guidance for determining the adequacy of data and preparing test plans used to prioritize chemicals for further work.

EPA will post this letter and the enclosed Comments on the HPV Challenge Web site within the next few days. As noted in the comments, we ask that The Synthetic Organic Chemical Manufacturers Association's Dibasic Esters Group advise the Agency, within 60 days of this posting on the Web site, of any modifications to its submission.

If you have any questions about this response, please contact Richard Hefter, Chief of the HPV Chemicals Branch, at 202-564-7649. Submit questions about the HPV Challenge Program through the HPV Challenge Program Web site "Submit Technical Questions" button or through the TSCA Assistance Information Service (TSCA Hotline) at (202) 554-1404. The TSCA Hotline can also be reached by e-mail at tsca-hotline@epa.gov.

I thank you for your submission and look forward to your continued participation in the HPV Challenge Program.

Sincerely,

-S-

Oscar Hernandez, Director
Risk Assessment Division

Enclosure

cc: W. Sanders
A. Abramson
C. Auer
M. E. Weber

EPA Comments on Chemical RTK HPV Challenge Submission:
Dibasic Esters Category

SUMMARY OF COMMENTS

The sponsor, the Synthetic Organic Chemical Manufacturers Association (SOCMA) submitted a test plan and robust summaries to EPA for the dibasic esters category on January 2, 2002. The test plan was posted on January 30, 2002. The category includes three dibasic esters: dimethyl succinate, dimethyl glutarate, and dimethyl adipate; and a mixture of the three.

EPA has reviewed this submission and has reached the following conclusions:

1. Category Justification. The category is clear and unambiguous. The submitter adequately supports the grouping of the category members with the information provided.

2. Physicochemical Properties and Environmental Fate. The submitter needs to indicate whether the submitted physicochemical data are calculated or measured. EPA prefers measured data for physicochemical properties. The submitter also needs to provide photodegradation data for DMG and address deficiencies in the biodegradation robust summary for DBE.

3. Health Effects. All appropriate SIDS-level endpoints have been addressed for the purposes of the HPV Challenge Program.

4. Ecological Effects. EPA reserves judgement on adequacy of the fish toxicity data pending clarification on the quantity of acetone used as a solvent in a key DMG study and submission of several required data elements missing from the robust summary. The daphnia and algae ECOSAR values are not adequate because no measured analog data are available that are consistent with SAR results. Therefore, the submitter needs to conduct daphnia and algal toxicity tests on one of the category members, preferably on DMA.

EPA requests that the submitter advise the Agency within 60 days of any modifications to its submission

EPA COMMENTS ON DIBASIC ESTERS CATEGORY CHALLENGE SUBMISSION

Category Definition

The submitter proposes a category covering three dibasic esters, dimethyl succinate (DMS, CAS No. 106-65-0), dimethyl glutarate (DMG, CAS No. 1119-40-0), and dimethyl adipate (DMA, CAS No. 627-93-0), and their mixture DBE (CAS No. 95481-62-2). A crude dibasic ester mixture is distilled to produce DMS, DMG, and DMA and three other fractions that are mixtures of these esters generally composed of 10-25, 55-65, and 15-25% DMA, DMG, and DMS, respectively. The category definition is clear and unambiguous, but the submitter's cover letter erroneously identifies dimethyl glutarate as dimethyl glutamate (an amino acid ester).

Category Justification

The category is based on similarity in structure, physicochemical properties, and toxicity responses. The three discrete compounds are all short four-to six-carbon straight-chain dicarboxylic acid dimethyl esters differing incrementally by one carbon atom. The four members of the category produce similar levels of acute and repeated-dose toxicity in experimental animals; therefore, information on one member of the category is expected to be representative of the toxicity of the category as a whole. However, for ecological effects, the submitter's analysis of quantitative structure-activity relationship (QSAR) failed to provide adequate justification for the submitter's conclusion that no further testing is necessary.

Test Plan

Physicochemical Properties (melting point, boiling point, vapor pressure, partition coefficient, and water solubility).

The submitter needs to indicate whether the submitted data are calculated or measured. EPA prefers that measured physicochemical property data be provided to characterize a substance and to provide accurate inputs to the transport-distribution model.

Environmental Fate (photodegradation, stability in water, biodegradation, fugacity).

The submitter did not provide photodegradation data for DMG.

The submitter used EPIWIN-generated physicochemical properties as inputs into the transport and distribution model. EPA recommends that the submitter use measured data as much as possible. The use of estimated values introduces uncertainties that then become magnified in modeling applications.

Health Effects (acute toxicity, repeated-dose toxicity, genetic toxicity, and reproductive/developmental toxicity).

The submitted data for all health effects endpoints are adequate for the purposes of the HPV Challenge Program.

Ecological effects (fish, invertebrates, and algae).

The quantitative structure-activity relationships (QSAR) analysis failed to provided adequate justification for the submitter's conclusion that no further testing is necessary.

Fish. The submitted data on DMA were inadequate because the study was of shorter duration (43 hrs) than the required 96 hrs. Studies on DBE and DMS provided LC_{50} results as ranges. The OECD guidelines and EPA guidance on robust summaries state that definitive LC_{50} values should be provided. In the Dupont 1976 DMG study, there appears to be an excessive use of acetone as a solvent (0.1 ml/ml). Pending receipt of clarification on the amount of acetone used and calculations of definitive LC_{50} values, EPA reserves judgement on the adequacy of the data for this endpoint.

Daphnia. The submitted data are only for the mixture, DBE, and are inconsistent with the predicted values for the other category chemicals. EPA therefore believes that the results of the DBE studies cannot be extrapolated to the single chemicals of the category and considers that this endpoint has not been adequately addressed. Furthermore, tests were performed on a mixture containing as little as 10% of DMA, the member expected to be the most toxic, and thus the estimated value for DMA (497 mg/L vs. the measured value of 136 mg/L for DBE) appears to underestimate significantly the true toxicity. Measured data for DMA are needed to clarify the situation and help interpret the DBE data. Therefore, EPA recommends that the submitter conduct a daphnia toxicity study on DMA and use the results of this study for read-across purposes. Also, the submitter needs to provide the nominal concentrations and corresponding measured concentrations used in the Monsanto 1992 DBE study and missing information on several critical elements in the robust summaries.

Algae. For the reasons stated above, EPA recommends conducting an algal toxicity study on DMA because the ECOSAR data are not adequate. No data are available for the mixture.

Specific Comments on the Robust Summaries

Secondary sources (IUCLID data) were used for some of the entries and study details were not provided. In these cases the original studies should be identified and the robust study summaries revised.

Environmental Fate

Biodegradation. For the DBE biodegradation robust summary, the submitter needs to provide source and

concentration of the microbial inoculum, initial concentration of the test chemical, and total degradation at the end of the test.

Ecological Effects.

General: All SAR predictions must include input values and accompanying measured data for an analog for the same endpoint to be considered adequate for the purpose of the Challenge Program.

DBE

Fish. The submitter needs to provide a definitive LC_{50} value instead of ranges. Missing data elements include chemical purity, type of test method (closed or open system, static or flow-through), and results of water quality criteria.

Daphnia. Missing data elements include pH, water hardness, dissolved oxygen, test substance purity, type of test method (closed or open system, static or flow-through), and nominal and measured concentrations. In addition, percent loss must be reported, if any.

DMS

Fish. The submitter needs to provide a definitive LC_{50} value instead of a range. The missing data elements include percent chemical purity, water hardness, temperature, and type of test method (closed or open system, static or flow-through).

DMG

Fish. The missing data elements include pH, dissolved oxygen, water hardness, percent chemical purity, and type of test method (closed or open system, static or flow-through).

Follow up Activity

EPA requests that the submitter advise the Agency within 60 days of any modifications to its submission.